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RESEARCH ARTICLE

DEVELOPMENT AND CHARACTERIZATION OF MEDICATED ORAL JELLIES OF PALONOSETRON HYDROCHLORIDE

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Abstract

Aim and objective: Dysphagia is one of the most common diseases mainly in geriatric and podiatric populations. As swallowing is the main difficulty in dysphagic patients, in that situation medicated jelly preparations are the best alternative to conventional doses forms (tablets and capsule doses form). This research article is aimed at the formulation and evaluation of Palonosetron hydrochloride oral jelly to avoid swallowing related issues in paediatric and geriatric patients and to improve its bioavailability.
Methods: Two methods i.e., congealing and heating were chosen to prepare sucrose-based jellies. All prepared formulation were evaluated on different parameters like physical appearance, drug content, pH and dissolution study, stability study etc.
Results: All formulation was found free from any type of gritty particles. Out of all formulations MJ1 was found best formulation on the basis of drug release profile i.e., 79.22% within 30 mins. Accelerated stability studies also confirmed that MJ1 and MJ2 are the best formulations.
Conclusion: This study concludes that Palonosetron hydrochloride can be delivered successfully by the means of jellies to avoid first pass metabolism.
Keywords: Dysphasia, medicated jellies, Palonosetron hydrochloride, stability studies.

INTRODUCTION

Patient compliance and easy dose administration are the two major concerns to be considered during drug dose development. Tablets and capsules are not a good choice for patients suffering from swallowing problems, especially in the geriatric and paediatric populations and dysphagic patients. Medicated jellies can provide ease of administration for such a population by overcoming the main problem[1]. Jellies are semisolid to thick viscous fluids which is easily taken by patients of advanced age, patients with disability in ingestion of food and drink in other word those having difficulty in mastication and swallowing. These can be administered without water or any type of liquid. Medicated jellies rapidly melt in the oral cavity at 37°C. During chewing medicated jelly rapidly releases drug which is rapidly absorbed through saliva and directly enters systemic circulation, bypassing first-pass metabolism[2].

Palonosetron hydrochloride is one of the most potent drugs to minimize "delayed chemotherapy-induced nausea and vomiting" one of the side effects of chemotherapy that occurs after more than 24 hours of therapy[3]. The molecular weight of palonosetron is (332.87) both hydrophilic and lipophilic in nature, with a half-life of 40 hours, approx. 62% protein binding. With all these good drug properties palonosetron is a drawback of poor bioavailability i.e., (50%)[4].

This study is aimed to develop medicated oral jelly formulations of Palonosetron hydrochloride for ease of administration in paediatrics and geriatric patients and to improve its bioavailability by avoiding first pass metabolism. Earlier few attempts were made on jellies as swallowing aids[5].

MATERIALS AND METHODS

Palonosetron hydrochloride was obtained from Incepta pharmaceutical, Ltd. Trisodium citrate and Glycerine were obtained from Square pharmaceutical Ltd. Citric acid and Methyl paraben were obtained from ACME Laboratories Ltd.

Formulation of medicated jellies loaded with Palonosetron hydrochloride:

Heating and congealing methods were used to formulate jellies. 66.7 gm of sugar is taken in beaker a to form a sugar syrup, with the addition of 100 ml of water. All ingredients which are listed in table number 1 were weighed accurately and mixed properly. Which is heated at 80°C temperature with continuous stirring. After complete dissolution of gelling agent citric acid and stabilizer were added which is followed by stirring, which will improve the softness of the jellies, followed by boiling for few a minutes with maintaining pH. Preservatives were added to the solution with proper mixing. The next step was the addition of a drug i. e. Palonosetron hydrochloride into the solution. The drug was weighed accurately and added to the above solution with proper mixing. In the last step drug-loaded solution was transferred into jellies moulds to cool down and transform in the forms of jellies. Moulds were covered properly to avoid any type of contamination[6-9].

Table 1: Different formulationsof Palonosetron hydrochloride loaded medicated jellies.

Ingredients (in %)	MJ1	MJ2	MJ3	MJ4
Xanthan gum	-	0.5	1	0.8
Trisodium citrate	3.3	3.0	2	2.8
Glycerin	3	3	3	3
Citric acid	2	-	2	-
Methyl paraben	0.18	0.18	0.18	
Sucrose	50	50	50	50
Sodium benzoate	0.01	0.01	0.01	0.01
Strawberryflavour	0.1	0.1	0.1	0.1
Water	20	20	20	20

Evaluations of Palonosetron hydrochloride-loaded jellies

Physical observation

All Palonosetron hydrochloride-loaded jellies were analysed for different types of physical testing like the texture of jellies (on the bases of stickiness and any type of grittiness by rubbing between fingers type of change in odor and visually analyzed for clarity[10,11].

Weight variation

For the estimation of variation in weight, ten jelly formulations were taken and weighed to find out average weight. A variation was monitored from average weight and individual weight[12,13].

Determination of pH

With the means of digital pH meter, pH of the formulations was estimated. Jelly was dissolved in water and after it pH was observed[14,15,16].

Spreadability

To determine the spreadability of drug-loaded jellies multimer suggested apparatus was used after fabrication. It was estimated based on the slides separation having jelly formulation[17,18,19].

Determination of viscosity

Viscosity of the prepared jelly formulations was measured by the means of Brookfield viscometer[20].

Content uniformity

Prepared jelly formulations were dissolved in 50 ml of phosphate buffer pH 6.8. Absorbance was measured by the means of UV visible spectrophotometer[21].

Syneresis

Syneresis or de-swelling is a characteristic of gels by releasing of liquid which cause shrinkage of gels resulting in quality reduction of formulation[22].

***In-vitro* dissolution study**

USP paddle-type apparatus was used for this study. Phosphate buffer was used as dissolution medium (900ml), temperature was maintained at 37°C and 100 rpm. Samples withdrawn periodically and absorbance is checked by means of UV visible spectro-photometer[22].

Kinetic modeling of dissolution data

Drug release kinetics were analyzed by various mathematical models such as a zero-order and first-order kinetic models; Higuchi and Korsmeyer–Peppas models to ascertain the kinetics of drug release[17].

Zero order kinetics

$$Q_1 = Q_0 + K_0 t$$

Where Q is the amount of the drug dissolved in time *t*, Q is the initial amount of drug in the solution (most times, Q_{50}) and *K* is the zero order release constant[23].

First order kinetics

$$\ln Q_t = \ln Q_0 - K_1 t$$

Where Q_t is the amount of drug released in time *t*, Q_0 is the initial amount of drug in the solution and *K* is the first order release constant.

Higuchi model

$$Q_t = K_H t_{1/2}$$

Where Q_t is the amount of drug released in time *t*, K_H is release rate constants.

Korsmeyer–Peppas model

$$Q_t/Q_\infty = at^n$$

Where *n* is the release exponent and the function of *t* is Q_t/Q_∞ (fractional release of the drug).

Stability studies

A physically stable oral gel retains its viscosity, color, clarity, taste, and odor throughout its shelf-life. The samples were kept at different temperatures (0-8°C and at room temperature) for 3 months. The samples of jellies were observed for pH, viscosity and appearance at the interval of one month. All the measurements were performed after allowing the samples to be equilibrated at 25°C for 2 h.

Statistical analysis

All experiments were done in triplicate for each sample; the results were presented as mean ± standard deviation. One-way analysis of variance analysis was employed to identify significant differences between data. Data were analyzed by omitting the insignificant term with probability value (p) ≤0.05.

RESULTS AND DISCUSSION

Total 4 jellies of Palonosetron hydrochloride were successfully prepared using xanthan gum, glycerin, citric acid, trisodium citrate and other ingredients in different ratio. Physical observation of jellies is important to justify the patient acceptance and compliance of the products. The medicated jelly was examined for physical appearance in terms of color, texture, clarity, and consistency. Among all the formulations MJ1 was found best with regards of smoothness and softness, MJ1 was found a little sticky but is within an acceptable limit. MJ2 formulation showed fluid-like consistency. MJ3 and MJ4 preparation were thick in consistency. The consistency and viscosity of the soft gels are co-related to each other because both are dependent on concentration of Xanthan gum, pectin sodium citrate, and co-solute. The concentration of the polymer directly influenced the viscosity.

Table 2: Outcomes of evaluation parameters of different drug loaded jelly preparations.

Batch	Appearance	Consistency	%Drug content	% Weight variation	pH	Viscosity (cps)	Spreadability	Syneresis
MJ1	Smooth and very soft	Cloudy	98.06±0.53	4.46±0.34	6.61±0.07	589937	24	6.48±0.08
MJ 2	Smooth and firm	Cloudy	98.32±0.36	5.68±0.25	6.63±0.06	633422	28	6.35±0.02
MJ 3	Smooth	Transparent	97.23±0.38	5.43%±0.08	6.72±0.07	707869	25	6.62±0.05
MJ 4	Very soft	Transparent	98.52±0.66	5.33%±0.12	6.83±0.02	658924	30	6.83±0.07

n=3, $p \leq 0.05$

Weight variation was found between 4.46±0.34% and 5.68±0.25% in all prepared jelly formulations. The pH of the drug-loaded preparations was found in the range of 6.22±0.02 to 6.63±0.06 which was slightly acidic. The pH of the jelly preparation in the form of solution just before gelation is adjusted by means of citric acid preferably to 4.0 or more up to 7.0. This is because when pH is below 4 jelly preparation liable to cause syneresis and stability of the preparation deteriorates in some cases. When the pH is 6 or more (close to neutrality), the jelly preparation is far more excellent in stability. Sucrose may cause precipitation with citric acid on standing[14]. Therefore, a minimum amount of citric acid was added just to maintain the pH.

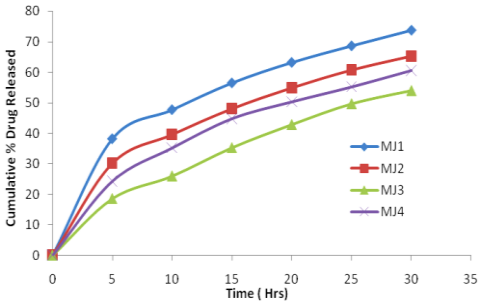

Figure 1: *In-vitro* release of medicated jellies.

The drug content of all the batches was in between 97.23±0.38 to 98.52±0.66, which is well within acceptable limits. Syneresis was checked after 24 h of the jelly formulation. No formulation showed syneresis at room temperature (25±5°C). Syneresis is more pronounced in the gels where lower concentration of gelling agent is used. Syneresis was not noticed at room temperature probably due to binding of free water by co-solute. The batch MJ1 has shown 79.22% and batch MJ2 has shown 71.65 % release within 30 min. The results of release kinetics from revealed that a higher coefficient of determination value (R^2 = 0.9784) was for first-order kinetic of the formulation MJ3 (Table 3). While the fitting of the drug released data on Korsmeyer–Peppas model showed non-fickain mechanism of drug transport (n value between 1.304 and 1.520) that assumed the drug releasing depends on both diffusion and polymer swelling with the time. The jelly formulations of batch MJ1 and MJ2 were checked for a change in various parameters for example appearance, pH, and viscosity for 3 months. The result depicts no significant changes in pH and appearance in the optimized jelly formulations of batches MJ1 and MJ2 with time. Formulation MJ1depicts best results.

Limitation of the study: There is need of *in-vivo* study for the estimation of the effectiveness of the prepared formulations.

Table: 3 *In-vitro* release kinetics data of drug loaded jellies.

Batch	Zero order		First order		Higuchi		Korsmeyer Peppas	
	r^2	K0(h-1)	r^2	K1(h-1)	r^2	KH(h-1/2)	r^2	n
MJ1	0.813	2.611	0.945	-0.034	0.970	16.39	0.968	1.431
MJ 2	0.823	2.723	0.969	-0.044	0.975	17.03	0.956	1.461
MJ 3	0.798	2.746	0.986	-0.048	0.969	17.39	0.968	1.520
MJ 4	0.902	2.703	0.967	-0.034	0.962	16.29	0.968	1.304

Table 4: Stability studies results of drug loaded jellies.

Batch	Month	pH	Viscosity
MJ1	1	6.41±0.04	589937
	2	6.38±0.07	579834
	3	6.22±0.02	569430
MJ2	1	6.63±0.06	633422
	2	6.49±0.04	622420
	3	6.53±0.08	612220

CONCLUSIONS

Current study was an attempt to formulate and evaluate Palonosetron hydrochloride loaded jellies. Four formulations were formulated using the heating and congealing method. MJ1 was found best formulation among all formulations. The above study can be concluded in the successful delivery of Palonosetron in the form of jelly. Formulations MJ1, could be effectively employed for oral delivery of Palonosetron hydrochloride for pediatric, geriatric and dysphagic patients as alternatives to solid oral dosage forms with improved bioavailability.

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AUTHOR CONTRIBUTIONS

Islam MS: writing, gathered and analyzed data. **Mojumder TJ:** data analysis, report drafting. **Nawrin F:** editing, review. All authors revised the article and approved the final version.

DATA AVAILABILITY

Data will be made available on request.

CONFLICT OF INTEREST

None to declare.

REFERENCES

1. Robinson JR, Lee VH. Marcel Dekker: Conventional drug delivery system 1987; 2(3): 4-15.
2. Gomaa E, Ayoub MM. Vardenafil oral jellies as a potential approach for management of pediatric irritable bowel syndrome. Saudi Pharm J 2021; 29:955–62. *https://doi.org/10.1016/j.jsps.2021.07.020*
3. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals (14 ed.). Merck & Co. 2006;1206. ISBN 978-0-911910-00-1.
4. De Leon A (October 2006). Palonosetron (Aloxi): A second-generation 5-HT$_3$ receptor antagonist for chemotherapy-induced nausea and vomiting. Proceedings 19 (4): 413–6. *https://doi.org/10.1080/08998280.2006.11928210*
5. Yoshida M, Hazekawa M, Haraguchi T, Uchida T. Influence of swallowing Aids on the adsorption and palatability of Kremezin®. Chem Pharm Bull (Tokyo) 2011; 59:434-7. *https://doi.org/10.1248/cpb.59.434*
6. Kim KH, Jun M, Lee MK. Bioavailability of the common cold medicines in jellies for oral administration. Pharmaceutics 2020; 12:1073. *https://doi.org/10.3390/pharmaceutics12111073*
7. James S. Encyclopaedia of pharmaceutical technology gels and jellies. 3rd ed. London: Informa Healthcare; 2007; 1875 - 1889.
8. Almurisi SH, Doolaanea AA, Akkawi ME, *et al*. Formulation development of paracetamol instant jelly for pediatric use. Drug Dev Ind Pharm 2020; 46:1373–83. *https://doi.org/10.1080/03639045.2020.1791165*
9. Kristi S, Resident course in confectionery technology, Gelling agents for confection: Gelatin, pectin, and xanthum gum, and sodium alginate. National confectioners association, The University of Wisconsin 2001.
10. Hanawa T, Watanabe A, Tsuchiya T, Ikoma R, Hidaka M, Sugihara M. New oral dosage form for elderly patients. II. Release behavior of benfotiamine from silk fibroin gel. Chem Pharm Bull (Tokyo) 1995; 43:872–6. *https://doi.org/10.1248/cpb.43.872*
11. Verma BK, Pandey S, Arya P. Tablet granulation: Current scenario and recent advances. Universal J Pharm Res 2017; 2(5): 30-35. *https://doi.org/10.22270/ujpr.v2i5.RW1*
12. Mahdin ZH. Oral jellies for improving oral drug delivery in dysphagia. Al Mustansiriyah J Pharm Sci. 2020; 20:94–104. *https://doi.org/10.32947/ajps.v20i3.765*
13. Gomaa E, Ayoub MM. Vardenafil oral jellies as a potential approach for management of pediatric irritable bowel syndrome. Saudi Pharm J 2021; 29:955–962. *https://doi.org/10.1016/j.jsps.2021.07.020*
14. Rowe Raymond C, Sheskey Paul J. Weller, Handbook of Pharmaceutical Excipients; Fourth Edition 2003; 89-92:491-492.
15. Kakino Y, Hishikawa Y, Onodera R, Tahara K, Takeuchi H. Gelation factors of pectin for development of a powder form of gel, dry jelly, as a novel dosage form. Chem Pharm Bull 2017; 65:1035–1044. *https://doi.org/10.1248/cpb.c17-00447*
16. Javed H, Shah S. Formulation and evaluation of taste masked Doxycycline HCl medicated jelly. Der Pharmacia Sinica 2017; 8(2):33-39.
17. Elshafeey AH, El-Dahmy RM. A novel oral medicated jelly for enhancement of etilefrine hydrochloride bioavailability: *In vitro* characterization and pharmacokinetic evaluation in healthy human volunteers. Saudi Pharm J 2022. *https://doi.org/10.1016/j.jsps.2022.07.004*
18. Yokoyama H, Hirata A, Hamamoto H. Inventor. Biguanide drug containing jelly preparation US Patent No. US2007/0053939A1.2007 March 13.
19. Karaiskou SG, Kouskoura MG, Markopoulou CK. Modern pediatric formulations of the soft candies in the form of a jelly: Determination of metoclopramide content and dissolution. Pharm Dev Technol 2020; 25:20–27. *https://doi.org/10.1080/10837450.2019.1609499*
20. Kadhim ZM, Ali WK. Utilization of natural polymer in the preparation of oral jelly of Granisetron. Al Mustansiriyah J Pharm Sci 2019; 19(2). *https://doi.org/10.32947/ajps.19.02.00398*
21. Peter OI, Ifeoma UC. Design and evaluation of carbamazepine lozenzes. Universal J Pharm Res 2017; 2(5): 1-4. *http://doi.org/10.22270/ujpr.v2i5.R1*
22. Arifa Begum Sk, Padma SV, Anusha V, *et al*. Formulation and evaluation of pediatric oral soft jellies of salbutamol sulphate) Research J Pharmacy Tech 2018; 11:1-3. *https://doi.org/10.5958/0974-360X.2018.00899.5*